REMARKS

Applicants have amended claim 1 to correct a typographical error objected to by the Examiner. This amendments is editorial in nature and does not introduce new matter; its entry is respectfully requested. Applicants have amended claims 1-3 and introduced new claim 24 to more particularly point out preferred embodiments of the present invention. For example, claim 1 is now directed to a method of inhibiting an undesired MHC class I immune associated reaction. These amendments are supported at page 30, lines 8 – 19 of the specification. New claim 24 is specifically supported at page 30, lines 14 – 15. As such, these amendments do not introduce new matter and their entry is respectfully requested. New claims 18 – 23 are directed to another preferred embodiment of the invention, namely the use of an internal ribosome entry site (IRES) to force expression of the antibody. These claims are supported by pages 32 – 33 of the specification. More particularly, claims 18 and 19 are supported by page 32, line 27 – page 22, line 1; and claims 20 – 23 are supported by page 33, lines 24 – 33. As such, these amendments do not introduce new matter and their entry is respectfully requested.

The examiner has objected to claim 1. Applicants respectfully submit that the amendment to this claim has obviated this objection, and respectfully request its withdrawal.

Applicants appreciate the examiner's withdrawal of the rejection of the claims under 35 U.S.C. § 112, second paragraph.

Claims 1 – 5, 7, and 13 were rejected under 35 U.S.C. § 102 (b) as being anticipated by Marasco et al., WO 94/02610.

Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

While WO 94/02610 broadly teaches a generic method of using intrabodies, the present invention recognizes that certain intrabody targets pose specific challenges, and teaches specific solutions which are tailored to meet those challenges.

Anticipation requires that the reference teach all the steps of the claims – this has not been done. Applicants have amended the claims to explicitly claim preferred embodiments of the invention. The claims are directed to inhibiting an MHC Class I (MHC-I) reaction by introducing two genes into a cell, one encoding an intrabody and a second encoding an MHC-I analog, to prevent triggering a natural killer (NK) cell reaction (e.g. claims 1 and 24) and to using an IRES signal (e.g. claims 18-23)

Applicants respectfully submit that the amended claims are not anticipated by WO 94/02610 for the following reasons. WO 94/02610 generically teaches broad classes of intracellular molecules as intrabody targets, one of which is the class of MHC molecules. However, WO 94/02610 does not teach the specific steps of the present claims. The present specification teaches at page 30, lines 11 – 15, that a total knock out of certain targets, including members of the MHC-I pathway, can be deleterious to the cell because it can trigger an NK reaction. To deal with this specific problem, the specification also teaches that one solution to this scenario is to introduce a second gene into the targeted cell, to specifically avoid triggering an NK reaction while allowing a total knockout of the targeted gene. The specification further teaches that one example of such a gene useful for preventing an NK reaction is an MHC-I analog which lacks the intracellular signaling domain. In contrast, WO 94/02610 does not mention NK cells.

Another embodiment of the present invention addresses another specific challenge presented by the use of intrabodies. An IRES signal can be useful to force gene expression and to obtain the light and heavy chains in equal stoichiometric ratio, thereby permitting more effective assembly.

Accordingly, the specific embodiments of the present invention are in no way anticipated by the generic teaching of WO 94/02610. Accordingly, applicants respectfully submit that this rejection should be withdrawn.

Claims 1 -5, 7, and 13 were rejected under 35 U.S.C. § 102 (e) as being anticipated by any one of three issued U.S. patents to Marasco: US 6,329,173 (the '173), U.S. 6,004,940 (the '940), and 5,965,371 (the '371).

The specifications of the '173 patent and the '371 patent are related applications and therefore are similar to each other as well as to the WO 94/02610. As discussed above, these

applications do not teach the specific claim steps of inhibiting NK reactions or the use of IRES sequences. Accordingly, for all of the reasons above, the present application is not anticipated by the '173 or the '371 patent.

Accordingly, in view of the foregoing, applicants respectfully submit that claims 1 – 5, 7, and 13 comply with 35 U.S.C. § 102.

Claims 1, 7, 13, and 16 were rejected under 35 U.S.C. § 103 (a) as being unpatentable over WO 94/02610 in view of Germain.

Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

The combination of references does not suggest the precise control of undesired immune reactions claimed. While WO 94/02610 is generic to the present invention, it does not suggest inhibiting an NK cell reaction by introducing two genes into a cell, one encoding an intrabody and a second encoding an MHC-I analog, to prevent triggering a natural killer (NK) cell reaction.

Germain merely provides a review of what was known at the time about the structure of MHC class I molecules. Merely knowing the structure of MHC class I molecules, as provided by Germain, in no way renders these specific preferred embodiments, nor the solutions offered by the present invention. Thus, applicants respectfully submit that the present invention would not have been obvious to the skilled artisan. Accordingly, this rejection should be withdrawn.

Claims 1, 7, 13, and 16 were rejected under 35 U.S.C. § 103 (a) as being unpatentable over any one of the '173 patent, the '940 patent, or the '371 patent in view of Germain.

Applicants respectfully submit that this rejection should be withdrawn for all of the reasons presented above. As discussed, the '173 and the '371 Marasco patents teach a generic concept; the '940 Marasco patent teaches an alternative specific embodiment. Germain merely provides a review of the state of the art regarding the structure of MHC class I molecules. None of these references, alone or in combination, contemplates the explicit method of the present invention, namely preventing an NK cell reaction while inhibiting an MHC Class I (MHC-I) reaction by introducing two genes into a cell, one encoding an intrabody **and a second encoding**

an MHC-I analog, to prevent triggering a natural killer (NK) cell reaction. Accordingly, this rejection should be withdrawn.

Accordingly, in view of the foregoing, applicants respectfully submit that all claims comply with 35 U.S.C. § 102.

In view of the foregoing, applicant respectfully submits that all claims are in condition for allowance. Early and favorable action is requested.

In the event that any additional fees are required, the PTO is authorized to charge our deposit account No. 50-0850.

Respectfully submitted,

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